# Supplementary Information

## Supplementary Methods

***Plasma sample preparation and analysis by GC-TOFMS*.** Plasma metabolite extraction and analysis were performed following our previously published procedure (1, 2) with minor modifications. Each 50 µL aliquot of plasma sample was spiked with two internal standard solutions (10 µl p-chlorophenylalanine in water, 0.1 mg/mL; 10 µL heptadecanoic acid in methanol, 1 mg/mL). The mixed solution was extracted with 175 µL of methanol: chloroform (3:1) and vortexed for 30 seconds. After storing for 10 minutes at −20°C, the samples were centrifuged at 13,000 rpm for 10 minutes. An aliquot of 200 µL supernatant was transferred to a glass sampling vial to vacuum dry at room temperature. The residue was derivatized using a two-step procedure. First, 50 µL methoxyamine (15 mg/mL in pyridine) was added to the vial and kept at 30°C for 90 minutes. After adding 10 µL C10-C40 (all even alkanes, 12.5 µg/mL) as retention index, 50 µL N,O-bis-(trimetylsilyl) trifluoroacetamide (BSTFA) (1% trimethylchlorosilane, TMCS) was added to the samples, before maintaining at 70°C for 60 minutes.

Each 1 µL aliquot of the derivatized solution was injected in splitless mode into an Agilent 6890N gas chromatography coupled with a Pegasus HT time-of-flight mass spectrometry (Leco Co., St. Joseph, MI, USA). To minimize systematic analytical deviations, each control sample was separated by 1 PC sample. PC samples from different disease stages were also run evenly in the whole experiment. Separation was achieved on an Rxi-5ms capillary column (Crossbond ® 5% diphenyl/95% dimethyl polysiloxane, Restek, PA, USA), with helium as the carrier gas at a constant flow rate of

1.0 mL/min. The temperatures of injection, transfer interface, and ion source were set to 260, 260, and 210°C, respectively. The GC temperature programming was set to 2 min isothermal heating at 80°C, followed by 10°C/min oven temperature ramped to 220°C, 5°C/min to 240°C, and 25°C/min to 290°C, and a final eight minute maintenance at 290°C. Electron impact ionization (70 eV) at full scan mode (*m/z* 40-600) was used, with an acquisition rate of 20 spectra/second in the TOFMS setting.

The data generated in the GC-TOFMS instrument were analyzed by the ChromaTOF software (v4.33, Leco Co., CA, USA). Using the statistic component, the aligned comma separated value (CSV) file can be obtained with sample information, peak information and peak intensity. Peak areas of unique mass were normalized to the internal standard. Compound identification was performed by comparing the mass fragments with NIST 05 Standard mass spectral databases in NIST MS search 2.0 (NIST, Gaithersburg, MD, USA) software with a similarity of more than 70% and reference standards (with retention time, or retention index if available in the library, as another parameter). Internal standards and any known artifactual peaks, such as peaks caused by noise, column bleed and BSTFA derivatization procedures, were removed from the dataset before statistical analysis.

***Plasma sample preparation and analysis by LC-TOFMS*.** Plasma sample preparation and analysis with LC-TOFMS was performed according to our published report (2-4). A volume of 50 µL supernatant was mixed with 200 µL mixture of methanol and acetonitrile (5:3) containing p-chlorophenylalanine as internal standard (5 µg/mL). The mixture was vortexed for 2 min, allowed to stand for 10 min, centrifuged at 13,000 rpm for 20 min, and the supernatant was used for LC-TOFMS analysis.

An Agilent HPLC 1200 system equipped with a binary solvent delivery manager and a sample manager (Agilent Corporation, Santa Clara, CA, USA) was used with chromatographic separations performed on a 4.6×150 mm 5 μm Agilent ZORBAX Eclipse XDB-C18 chromatography column. The column was maintained at 30°C and eluted with a 1–100% acetonitrile (0.1 % (v/v) formic acid)—aqueous formic acid (0.1 % (v/v) formic acid) gradient over 25 min at a flow rate of 0.4 mL/min. A 10 μL aliquot sample was injected onto the column. Mass spectrometry was performed using an Agilent model 6220 MSD TOF MS equipped with a dual sprayer electrospray ionization source (Agilent Corporation, Santa Clara, CA, USA). The system was tuned for optimum sensitivity and resolution using an Agilent ESI-L low concentration tuning mix in both positive (ES+) and negative (ES−) electrospray ionization modes. The Agilent API-TOF reference mass solution kit was used to obtain accurate mass time-of-flight data in both positive and negative mode operation. The TOF MS was operated under the following optimized conditions: (1) ES+ mode, capillary voltage 3500 V, nebulizer 45 psig, drying gas temperature 325°C, drying gas flow 11 L/min, and (2) ES− mode, similar conditions as ES+ mode except that capillary voltage was adjusted to 3000 V. The TOF MS is calibrated routinely in ES+ and ES− modes using the Agilent ESI-L low concentration tuning mix. During metabolite profiling experiments, both plot and centroid data were acquired for each sample from 50 to 1,000 Da over a 25-min analysis time.

The resulting raw data files were then centroided, deisotoped, and converted to mzData xml files using the MassHunter Qualitative Analysis Program (vB.03.01) (Agilent). Following the conversion, the xml files were analyzed using the open source XCMS package (v1.24.1) (http://metlin.scripps.edu), which runs in the statistical

package R (v.2.12.1) (http://www.r-project.org), to pick, align, and quantify features (chromatographic events corresponding to specific m/z values and retention times). The software was used with default settings as described (http://metlin.scripps.edu) except for xset (bw = 5) and rector (plottype = “m”, family = “s”). The created .tsv file was opened using Excel software and saved as .xls file. The resulting data sheet was normalized to the internal standard and used for further analysis. Metabolite annotation was performed by comparing the accurate mass (m/z) and retention time (Rt) of reference standards in our in-house library and the accurate mass of compounds obtained from the web-based resources such as the Human Metabolome Database (http://www.hmdb.ca/).

**References**

1. Bao Y, Zhao T, Wang X, Qiu Y, Su M, Jia W. Metabonomic variations in the drug-treated type 2 diabetes mellitus patients and healthy volunteers. J Proteome Res. 2009;8:1623-30.

2. Qiu Y, Cai G, Su M, Chen T, Zheng X, Xu Y, et al. Serum metabolite profiling of human colorectal cancer using GC-TOFMS and UPLC-QTOFMS. J Proteome Res. 2009;8:4844-50.

3. Xie G, Zhong W, Zheng X, Li Q, Qiu Y, Li H, et al. Chronic Ethanol Consumption Alters Mammalian Gastrointestinal Content Metabolites. Journal of Proteome Research. 2013;12:3297–306.

4. Chen T, Xie G, Wang X, Fan J, Qiu Y, Zheng X, et al. Serum and urine metabolite profiling reveals potential biomarkers of human hepatocellular carcinoma. Mol Cell Proteomics. 2011;10:M110 004945.

**Table S1.** List of 202 identified plasma metabolites by GC-TOFMS and LC-TOFMS in pancreatic cancer patients and controls from CT and SH.

| Metabolite | Platform | Database | m/z | Rt (min) |
|---|---|---|---|---|
| Propionylcarnitine | LC-MS | HMDB00824 | 218.1375 | 9.70 |
| 2,5-dihydroxybenzoic acid | LC-MS | Standard | 153.0189 | 16.87 |
| LysoPC(14:0) | LC-MS | HMDB10379 | 468.3072 | 21.51 |
| Uric acid | LC-MS | Standard | 169.035 | 4.78 |
| Talopyranose | GC-MS | NIST | 204 | 15.30 |
| Urea | GC-MS | Standard | 171 | 7.37 |
| Proline | GC-MS | Standard | 142 | 8.98 |
| Glutamate | GC-MS | Standard | 246 | 13.07 |
| Nicotinic acid mononucleotide | LC-MS | HMDB01132 | 336.0504 | 3.94 |
| Choline | LC-MS | Standard | 105.1019 | 3.46 |
| 2,4-Diaminobutyric acid | LC-MS | HMDB02362 | 119.085 | 4.00 |
| 1,5-Anhydro-D-glucitol | GC-MS | NIST | 259 | 15.72 |
| Tryptophan | LC-MS | Standard | 203.0794 | 13.91 |
| 1,3,7-Trimethyluric acid | LC-MS | HMDB02123 | 209.0626 | 3.78 |
| 2-Methyl-3-oxopropanoic acid | LC-MS | HMDB01172 | 101.0247 | 4.21 |
| Glutamine | GC-MS | Standard | 156 | 14.79 |
| Betaine | LC-MS | Standard | 118.087 | 4.01 |
| Monoisobutyl phthalic acid | LC-MS | HMDB02056 | 223.0945 | 19.78 |
| 3-Amino-2-piperidone | GC-MS | NIST | 128 | 11.09 |
| Indoleacrylic acid | LC-MS | HMDB00734 | 188.0705 | 13.89 |
| 2-Oxoglutaric acid | GC-MS | Standard | 198 | 12.54 |
| Indoleacetic acid | LC-MS | HMDB00197 | 176.0736 | 12.36 |
| Creatinine | GC-MS | Standard | 115 | 12.37 |
| Methylguanidine | LC-MS | Standard | 74.0594 | 3.67 |
| N-Acetylglutamine | LC-MS | HMDB06029 | 189.0865 | 3.82 |
| Galactitol | LC-MS | HMDB00107 | 183.0832 | 5.25 |
| 2-Hydroxycinnamic acid | LC-MS | HMDB02641 | 165.0537 | 5.26 |
| Adenine | LC-MS | Standard | 136.0745 | 5.22 |
| Glycocholic acid | LC-MS | Standard | 464.2869 | 18.97 |
| Valine | GC-MS | Standard | 144 | 7.83 |
| 2-Aminobutyric acid | GC-MS | Standard | 130 | 7.19 |
| Decosahexaenoic acid | GC-MS | Standard | 91 | 22.35 |
| Myo-inositol | GC-MS | Standard | 318 | 18.39 |
| Cysteine | GC-MS | Standard | 220 | 12.33 |
| Dihydrothymine | LC-MS | HMDB00079 | 129.0629 | 3.65 |
| Acetylcarnitine | LC-MS | Standard | 204.1218 | 3.98 |
| Glyceric acid | GC-MS | Standard | 189 | 9.46 |
| Ornithine | LC-MS | Standard | 133.087 | 3.19 |
| beta-D-Glucopyranuronic acid | LC-MS | HMDB10314 | 313.0559 | 3.63 |

| | | | | |
|---|---|---|---|---|
| Histidine | GC-MS | Standard | 154 | 16.36 |
| Aminocaproic acid | LC-MS | HMDB01901 | 132.1017 | 7.48 |
| 3-Methoxytyramine | LC-MS | Standard | 168.0903 | 11.32 |
| N-methyl-L-histidine | GC-MS | NIST | 96 | 15.17 |
| Gamma-linolenyl carnitine | LC-MS | HMDB06318 | 422.3249 | 20.73 |
| Alloisoleucine | LC-MS | Standard | 132.1016 | 8.67 |
| 3,4,5-Trimethoxycinnamic acid | LC-MS | HMDB02511 | 239.0924 | 17.37 |
| Threo-3-Phenylserine | LC-MS | HMDB02184 | 180.0649 | 5.40 |
| Nicotinate D-ribonucleoside | LC-MS | HMDB06809 | 255.0766 | 17.36 |
| Leucine | GC-MS | Standard | 158 | 8.62 |
| Glucose | GC-MS | Standard | 319 | 16.29 |
| Tyramine-O-sulfate | LC-MS | HMDB06409 | 216.0326 | 3.56 |
| phosphate | GC-MS | Standard | 299 | 8.70 |
| Threonine | GC-MS | Standard | 219 | 10.23 |
| Trimethylamine N-oxide | LC-MS | Standard | 76.0734 | 3.57 |
| Arabitol | GC-MS | Standard | 217 | 14.36 |
| Sphingosine | LC-MS | HMDB00252 | 300.2888 | 20.54 |
| 4-Methyl-2-oxovaleric acid | LC-MS | Standard | 129.0553 | 16.83 |
| Indole-5,6-quinone | LC-MS | HMDB06779 | 148.0393 | 4.78 |
| Hippuric acid | LC-MS | Standard | 180.0658 | 16.51 |
| 2-oxo-4-methylvaleric acid | GC-MS | NIST | 89 | 7.78 |
| Citrulline | LC-MS | Standard | 176.1093 | 3.57 |
| Ribose, 5-phosphate | GC-MS | NIST | 211 | 19.81 |
| Delta-hydroxylysine | LC-MS | Standard | 163.114 | 3.54 |
| Carnitine | LC-MS | Standard | 162.1114 | 3.54 |
| Ribose | GC-MS | NIST | 103 | 13.71 |
| Phosphoserine | LC-MS | Standard | 186.019 | 3.10 |
| Aminoadipic acid | GC-MS | NIST | 260 | 12.31 |
| Oxalosuccinic acid | LC-MS | HMDB03974 | 189.0027 | 17.17 |
| Lysine | GC-MS | Standard | 156 | 16.35 |
| 4-Hydroxy-proline | GC-MS | Standard | 140 | 11.99 |
| 3-Methylcrotonylglycine | LC-MS | HMDB00459 | 158.0806 | 12.06 |
| Arachidonic acid | GC-MS | Standard | 91 | 21.07 |
| 11-Ketoetiocholanolone | LC-MS | HMDB06031 | 305.215 | 3.59 |
| 2-Methylacetoacetic acid | LC-MS | HMDB03771 | 115.0399 | 10.79 |
| 3-Methyluridine | LC-MS | HMDB04813 | 257.0739 | 4.96 |
| 3-Pyridylacetic acid | LC-MS | Standard | 138.0522 | 3.70 |
| Threonic acid | GC-MS | Standard | 73 | 12.47 |
| Glutaric acid | GC-MS | Standard | 147 | 10.34 |
| Glycerophosphocholine | LC-MS | HMDB00086 | 258.1108 | 3.50 |
| Tyrosine | GC-MS | Standard | 218 | 16.53 |
| Indole | LC-MS | HMDB00738 | 116.0503 | 13.91 |
| 4,8-dimethylnonanoyl carnitine | LC-MS | HMDB06202 | 330.2632 | 19.15 |
| Urocanic acid | LC-MS | Standard | 139.053 | 4.19 |

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|---|---|---|---|---|
| 3,4-Dehydro-DL-proline | LC-MS | Standard | 114.0593 | 3.65 |
| 5-Oxoproline | GC-MS | Standard | 156 | 11.91 |
| Stearoylcarnitine | LC-MS | HMDB00848 | 428.3716 | 22.49 |
| Cholesterol | GC-MS | Standard | 129 | 27.77 |
| Phenylalanine | GC-MS | Standard | 218 | 13.17 |
| Normetanephrine | LC-MS | Standard | 184.092 | 3.56 |
| LysoPC(18:0) | LC-MS | HMDB10384 | 524.3696 | 22.04 |
| LysoPC(20:3(5Z,8Z,11Z)) | LC-MS | HMDB10393 | 546.354 | 19.01 |
| LysoPC(16:0) | LC-MS | HMDB10382 | 496.3391 | 20.24 |
| 3-Oxodecanoic acid | LC-MS | HMDB10724 | 185.1154 | 20.51 |
| Benzoic acid | GC-MS | Standard | 179 | 8.22 |
| Methionine | GC-MS | Standard | 176 | 11.87 |
| Guanidineacetic acid | LC-MS | Standard | 116.0391 | 4.10 |
| 2-Deoxytetronic acid | GC-MS | NIST | 73 | 10.79 |
| 3-methyl-3-hydroxybutanoic acid | GC-MS | NIST | 131 | 7.71 |
| Proline betaine | LC-MS | HMDB04827 | 144.0982 | 3.81 |
| Nicotinamide (niacinamide) | LC-MS | Standard | 123.0438 | 5.15 |
| Hexanoic acid | GC-MS | NIST | 173 | 5.68 |
| 3-Deoxytetronic acid | GC-MS | NIST | 103 | 10.54 |
| Isohomovanillic acid | LC-MS | HMDB00333 | 181.0484 | 14.20 |
| Mannitol | GC-MS | Standard | 205 | 16.63 |
| Phenylpropionylglycine | LC-MS | HMDB00860 | 206.0798 | 17.45 |
| Allocystathionine | LC-MS | HMDB00455 | 223.0738 | 20.90 |
| Gluconate | LC-MS | Standard | 195.0504 | 3.56 |
| Oxalic acid | GC-MS | Standard | 147 | 6.73 |
| Alanine | GC-MS | Standard | 116 | 6.17 |
| Methylcysteine | GC-MS | NIST | 218 | 10.65 |
| Asparagine | GC-MS | Standard | 116 | 13.67 |
| Heneicosanoic acid | GC-MS | NIST | 132 | 20.80 |
| 3-Deoxyarabinohexonic acid | LC-MS | HMDB00346 | 181.0714 | 12.10 |
| Glycerolphosphate | GC-MS | Standard | 299 | 14.75 |
| 4-Hydroxybutyric acid | LC-MS | HMDB00710 | 103.0403 | 9.50 |
| Malic acid | GC-MS | Standard | 147 | 11.51 |
| Xylose | GC-MS | Standard | 103 | 13.86 |
| 4-Deoxypyridoxine | GC-MS | NIST | 282 | 13.93 |
| 2-Hydroxybutyric acid | GC-MS | Standard | 131 | 6.53 |
| Uracil | LC-MS | Standard | 113.0209 | 4.83 |
| LysoPC(16:1(9Z)) | LC-MS | HMDB10383 | 494.3221 | 22.10 |
| 3-Methyl-2-oxobutyrate | GC-MS | Standard | 73 | 6.27 |
| Stearic acid | GC-MS | Standard | 117 | 19.75 |
| LysoPE(18:0/0:0) | LC-MS | HMDB11130 | 482.3226 | 20.64 |
| p-cresol | GC-MS | Standard | 165 | 6.86 |
| Fructose | GC-MS | Standard | 217 | 16.13 |
| Pyruvic acid | GC-MS | Standard | 174 | 5.38 |

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|---|---|---|---|---|
| 2,4-Dichlorophenol | LC-MS | HMDB04811 | 160.9587 | 3.15 |
| Ethylene glycol | GC-MS | NIST | 147 | 4.52 |
| 7-Ketocholesterol | LC-MS | HMDB00501 | 401.3439 | 21.67 |
| N-acetyl-L-tyrosine | LC-MS | Standard | 222.0749 | 14.40 |
| Citric acid | GC-MS | Standard | 273 | 15.36 |
| 2,3-Dihydroxybutanoic acid | GC-MS | NIST | 292 | 9.67 |
| LysoPC(18:2(9Z,12Z)) | LC-MS | HMDB10386 | 520.3378 | 22.85 |
| Lactic acid | GC-MS | Standard | 117 | 5.57 |
| Alpha-hydroxyisobutyric acid | GC-MS | Standard | 131 | 5.61 |
| Glyceraldehyde 3-phosphate | LC-MS | Standard | 171.0059 | 3.13 |
| Ethyltestosterone | LC-MS | HMDB06002 | 315.2351 | 22.94 |
| Aminomalonic acid | GC-MS | Standard | 218 | 11.29 |
| Levoglucosan | GC-MS | NIST | 204 | 15.61 |
| N-formyl-glycine | GC-MS | NIST | 160 | 11.14 |
| 3-Hydroxybenzoic acid | LC-MS | HMDB02466 | 137.0226 | 18.99 |
| Bilirubin | LC-MS | HMDB00054 | 585.2691 | 18.64 |
| Terephthalic acid | LC-MS | HMDB02428 | 167.0362 | 23.67 |
| cis-5-Tetradecenoylcarnitine | LC-MS | HMDB02014 | 370.2988 | 20.21 |
| Beta-alanine | GC-MS | Standard | 174 | 10.71 |
| 3-Methyladipic acid | LC-MS | HMDB00555 | 159.0689 | 3.76 |
| Isoleucine | GC-MS | Standard | 158 | 8.94 |
| 2-Hydroxy-2-methylbutyric acid | LC-MS | Standard | 117.0555 | 13.76 |
| Succinic acid | GC-MS | Standard | 147 | 9.14 |
| Palmitoylcarnitine | LC-MS | Standard | 400.3407 | 21.67 |
| Glycine | GC-MS | Standard | 174 | 9.12 |
| Hydroxyisocaproic acid | LC-MS | Standard | 131.0691 | 17.04 |
| Isovalerylsarcosine | LC-MS | HMDB02087 | 172.0959 | 17.01 |
| Arginine | LC-MS | Standard | 175.1155 | 3.44 |
| Gamma-glutamyl-L-leucine | LC-MS | HMDB11171 | 261.1435 | 14.12 |
| Myristic acid | GC-MS | Standard | 117 | 15.44 |
| 3-Hydroxybutyric acid | GC-MS | Standard | 117 | 7.00 |
| Hydroxyacetic acid | GC-MS | Standard | 73 | 5.75 |
| 1-stearoyl-rac-glycerol | GC-MS | NIST | 399 | 23.80 |
| kynurenine | LC-MS | Standard | 209.0901 | 11.25 |
| Palmitoleic acid | GC-MS | Standard | 117 | 17.28 |
| 2-Hydroxy-3-methylbutyric acid | GC-MS | Standard | 145 | 7.09 |
| Linoleic acid | GC-MS | Standard | 337 | 19.40 |
| 3-Octenoic acid | GC-MS | NIST | 199 | 5.70 |
| Phenol | LC-MS | HMDB00228 | 93.03504 | 14.93 |
| Allantoin | GC-MS | NIST | 314 | 12.09 |
| Ketoleucine | LC-MS | HMDB00695 | 129.0552 | 15.84 |
| N-acetylglycine | GC-MS | NIST | 144 | 9.91 |
| Palmitic acid | GC-MS | Standard | 117 | 17.49 |
| Palmitin | GC-MS | Standard | 371 | 22.53 |

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|---|---|---|---|---|
| Octanoylcarnitine | LC-MS | HMDB00791 | 288.2166 | 17.96 |
| Dodecanoylcarnitine | LC-MS | HMDB02250 | 344.2798 | 19.78 |
| Oleic acid | GC-MS | Standard | 339 | 19.45 |
| Pseudo uridine | GC-MS | NIST | 217 | 21.04 |
| 3-Methyl-2-oxovalerate | GC-MS | Standard | 89 | 7.29 |
| 1,5-anhydroglucitol (1,5-AG) | GC-MS | NIST | 217 | 15.15 |
| Decanoylcarnitine | LC-MS | Standard | 316.2477 | 18.85 |
| 2,3,4-Trihydroxybutyric acid | LC-MS | Standard | 137.0462 | 4.03 |
| Valerylglycine | LC-MS | HMDB00927 | 158.0807 | 14.44 |
| LysoPC(18:1(9Z)) | LC-MS | HMDB02815 | 522.3545 | 21.23 |
| Glycerol | GC-MS | Standard | 218 | 8.68 |
| Tetradecanoylcarnitine | LC-MS | HMDB05066 | 372.3116 | 20.82 |
| 2-Oxo-4-methylthiobutanoic acid | LC-MS | HMDB01553 | 149.0236 | 23.67 |
| Serine | GC-MS | Standard | 204 | 9.86 |
| Hypoxanthine | LC-MS | Standard | 137.0463 | 4.80 |
| Threitol | GC-MS | Standard | 217 | 11.83 |
| Nonanoic acid | GC-MS | Standard | 215 | 9.73 |
| Fumaric acid | GC-MS | Standard | 245 | 9.57 |
| Laurate | GC-MS | Standard | 257 | 13.32 |
| Decanoic acid | GC-MS | Standard | 117 | 10.99 |
| 9-octadecenoate | GC-MS | NIST | 339 | 19.53 |
| Nutriacholic acid | LC-MS | HMDB00467 | 391.2854 | 23.67 |
| Aspartic acid | GC-MS | Standard | 232 | 11.90 |
| Cystine | GC-MS | Standard | 146 | 20.60 |
| Tiglylglycine | LC-MS | HMDB00959 | 156.0662 | 12.10 |
| LysoPC(20:4(8Z,11Z,14Z,17Z)) | LC-MS | HMDB10396 | 544.3375 | 22.64 |
| Caprylic acid | GC-MS | Standard | 201 | 8.42 |
| Pyrrole-2-carboxylic acid | GC-MS | NIST | 240 | 9.22 |
| Deoxycorticosterone | LC-MS | Standard | 331.2472 | 21.12 |
| Hypotaurine | LC-MS | Standard | 110.0095 | 3.12 |
| 1-Salicylate glucuronide | LC-MS | HMDB10313 | 315.0695 | 3.66 |

**Table S2.** Logistic regression analysis reveals PC-associated plasma metabolomics signature was independent of the possible confounding risk factors including BMI, use of tobacco and alcohol, and age and sex.

| | Odds ratio (95% CI)[5] | S.E. | P value |
|---|---|---|---|
| PC-associated plasma metabolite signature | 237.153 (89.754-626.618) | 4.957E-01 | 2.696E-28 |
| BMI[1] | 0.994 (0.926-1.067) | 3.621E-02 | 8.665E-01 |
| history of smoking[2] | 1.001 (0.984-1.02) | 9.137E-03 | 8.719E-01 |
| history of drinking[2] | 1 (0.992-1.007) | 3.883E-03 | 9.636E-01 |
| Age[3] | 1.001 (0.742-1.351) | 1.528E-01 | 9.930E-01 |
| Sex[4] | 1.018 (0.531-1.95) | 3.317E-01 | 9.571E-01 |

P values were calculated using the Wald test.

[1]BMI is continuous variables. [2]Yes or No. [3]Age (40-55, 55-65, 65-75, 75-85). [4]male or female. [5]Odds ratios greater than 1 correspond to a possibility of PC as compared to the lower values of continuous variables or the reference group of categorical variables.

**Table S3**. Logistic regression analysis of six plasma metabolite signatures in CT.

| | Coefficient | S.E. | p value |
|---|---|---|---|
| **Glutamate** | -2.338 | 0.814 | 4.10E-03 |
| **Choline** | 4.730 | 1.343 | 4.31E-04 |
| **1,5-Anhydro-D-glucitol** | 4.288 | 0.845 | 3.93E-07 |
| **Betaine** | 4.636 | 1.627 | 4.38E-03 |
| **Methylguanidine** | -0.418 | 0.122 | 6.22E-04 |
| **Glycocholic acid** | -1.418 | 1.178 | 2.29E-01 |
| **Constant** | -8.711 | 2.132 | 4.38E-05 |

P values were calculated using the Wald test.

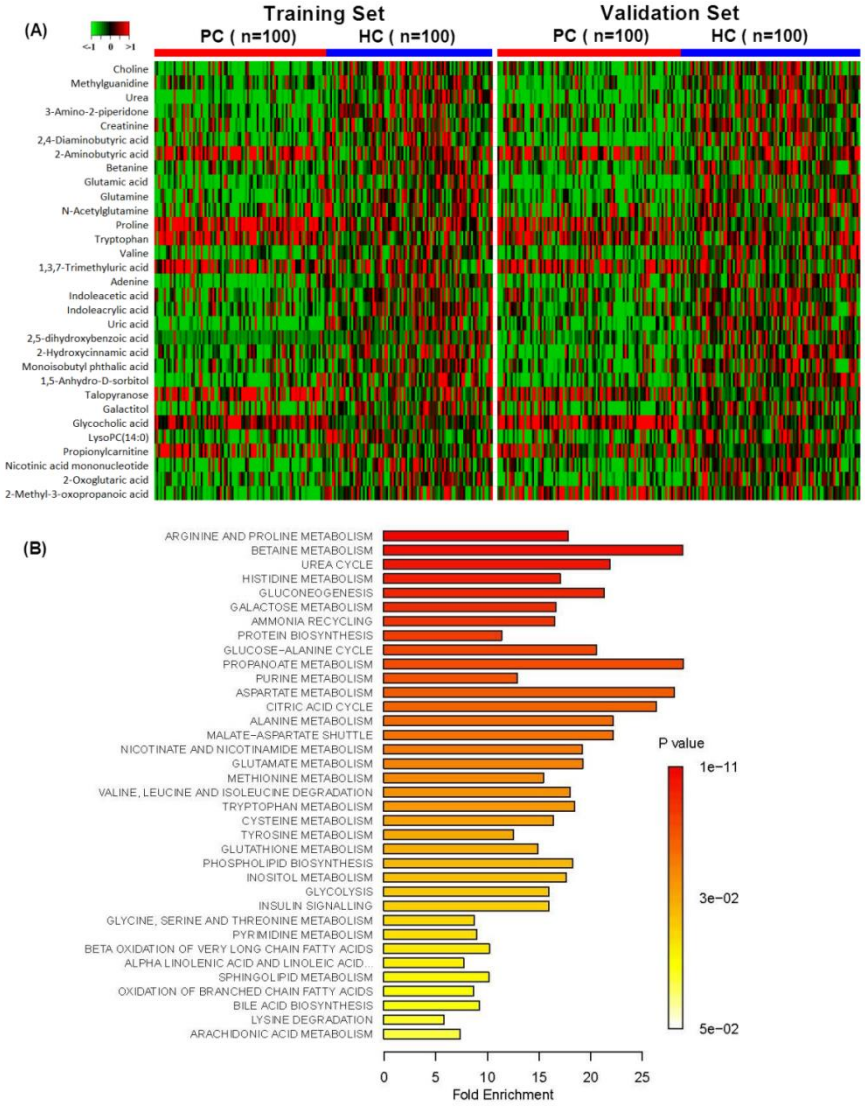


**Figure S1**. The total altered metabolites and altered metabolic pathways in PC.

(A) Heatmap representing 31 differential metabolites (adjusted P < 0.05) in the CT set and the SH set. Cells of heatmap represent median values of metabolites in the corresponding subjects. (B) Metabolite set enrichment analysis revealed 36 altered metabolic pathways in PC (P < 0.05).

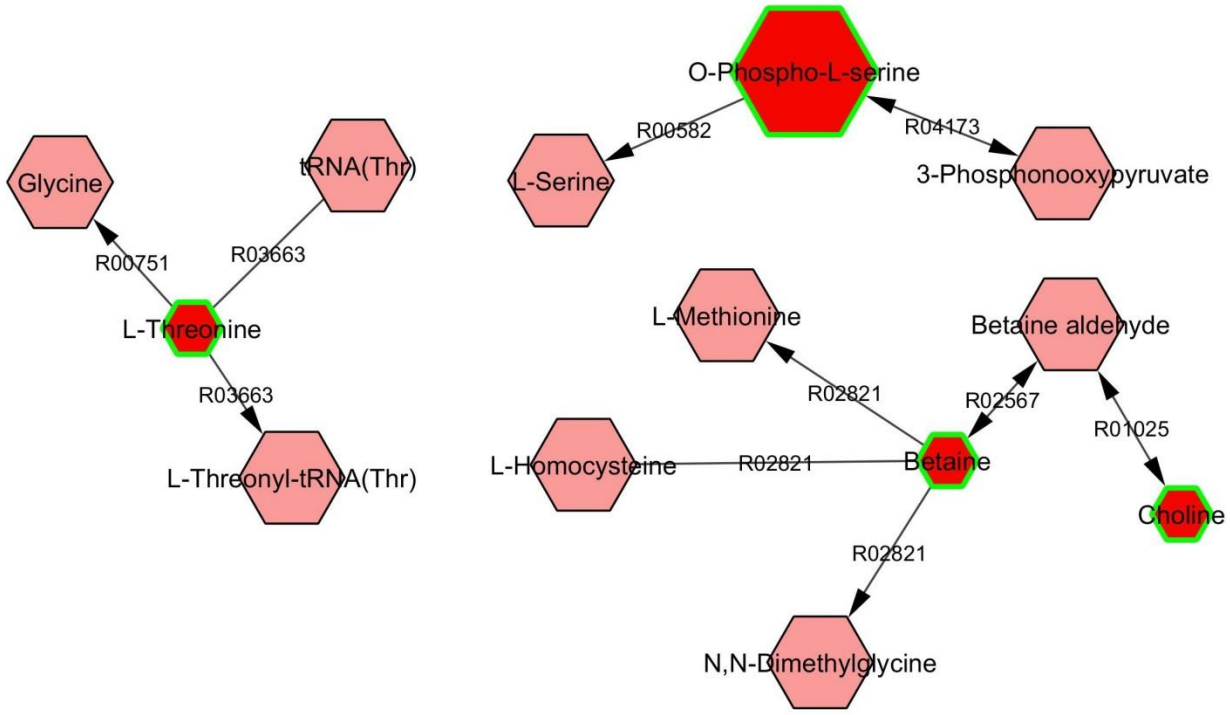


**Figure S2**. Glycine/serine/threonine/methionine metabolism of PC.

The detected metabolites in our study are represented by red hexagons. Hexagons with green lines means that the alteration of the metabolite in PC patients had statistical significance (*P* <0.05). The size of hexagons indicates the fold change of the corresponding metabolite in PC relative to control. In addition, pink hexagons indicate metabolites participating in the metabolic pathway but not been detected in the study.

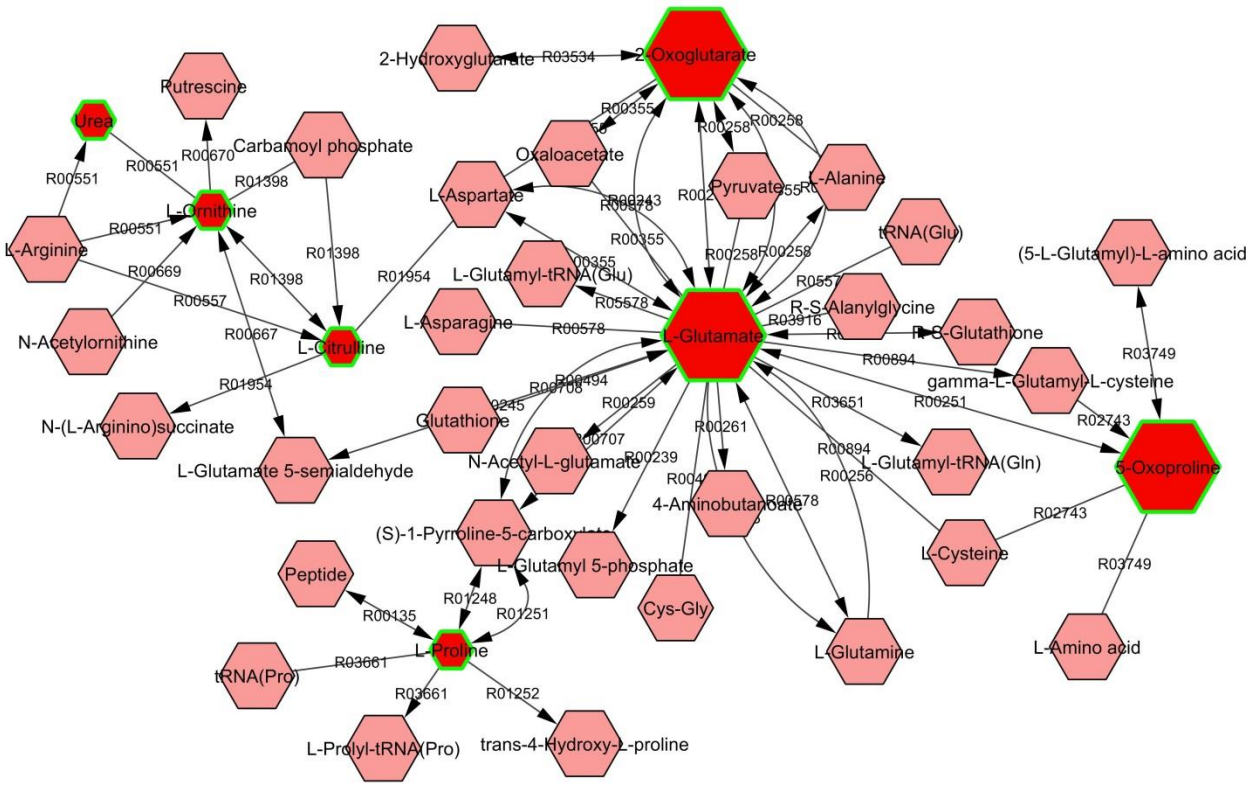


**Figure S3**. Glutamate pathway of PC.

Symbols are the same as in Figure S2.

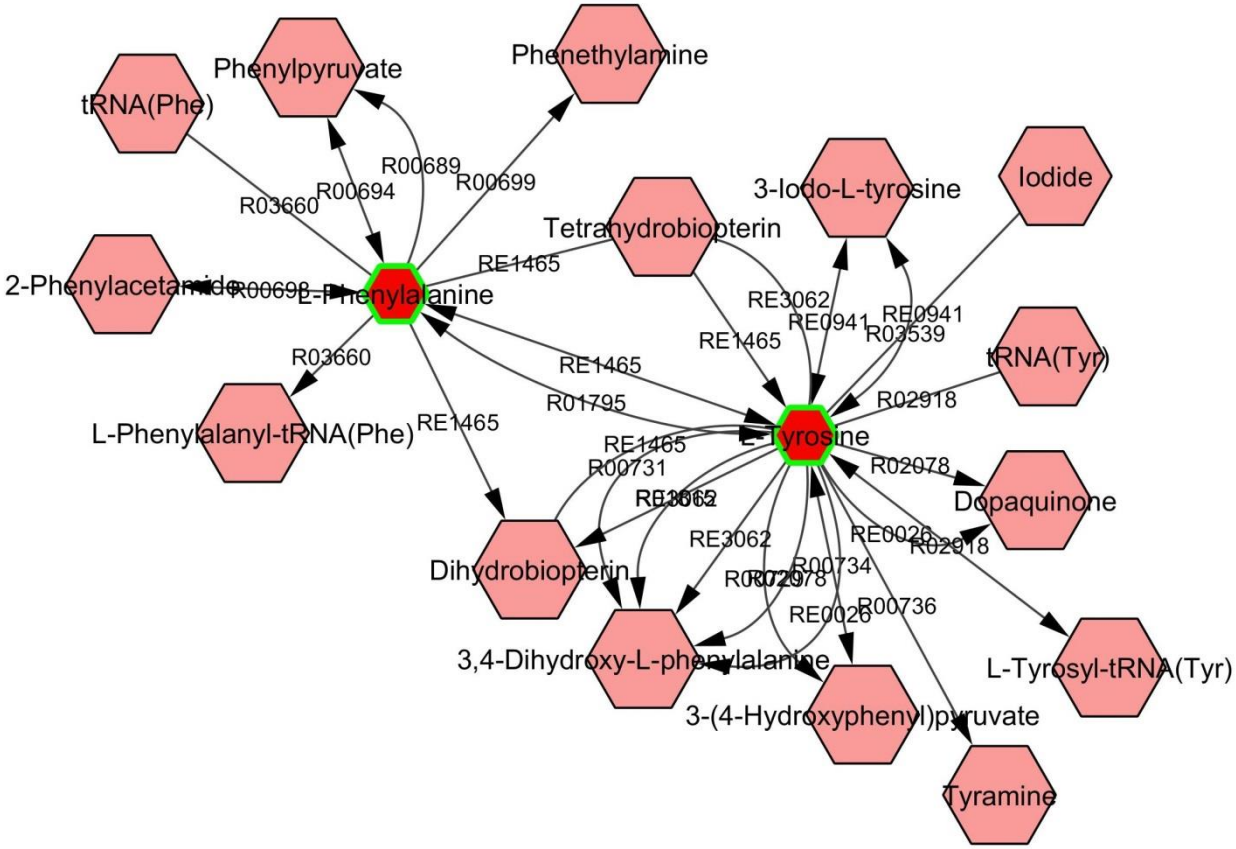


**Figure S4**. Tyrosine metabolism of PC.

Symbols are the same as in Figure S2.

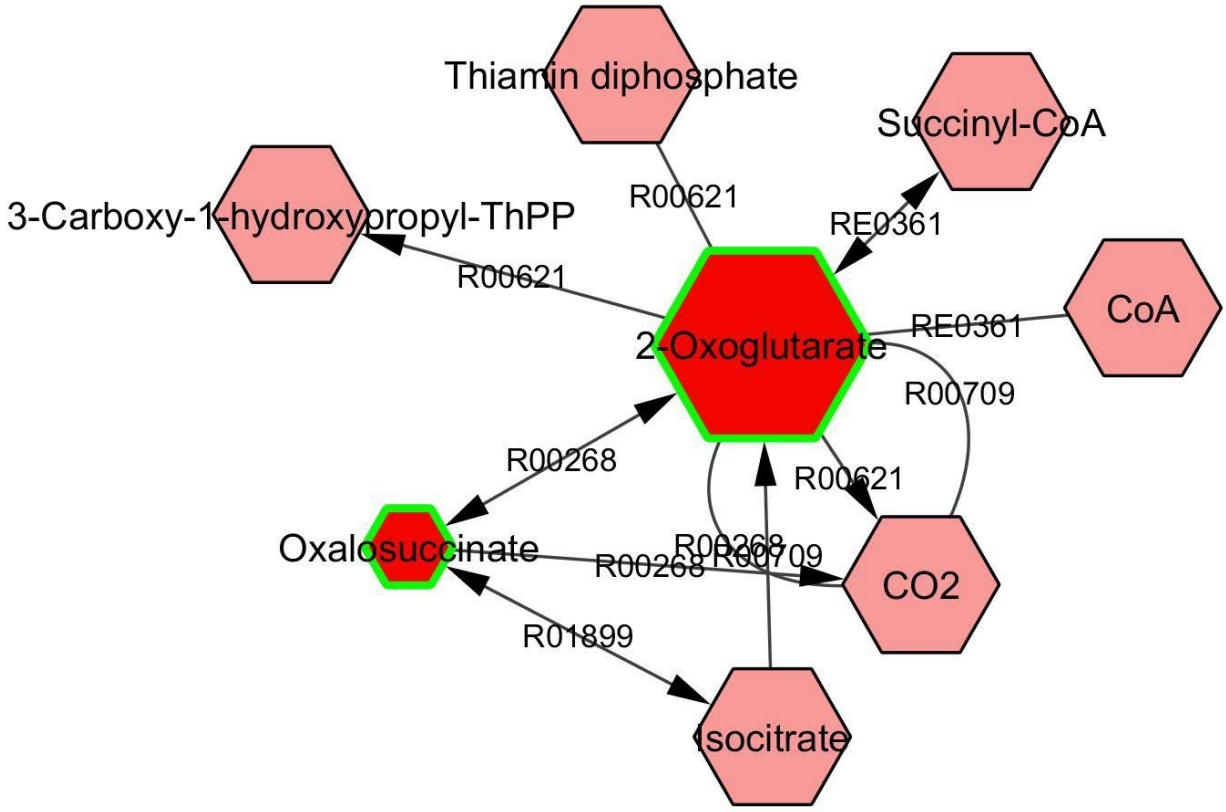


**Figure S5.** TCA cycle of PC.

Symbols are the same as in Figure S2.

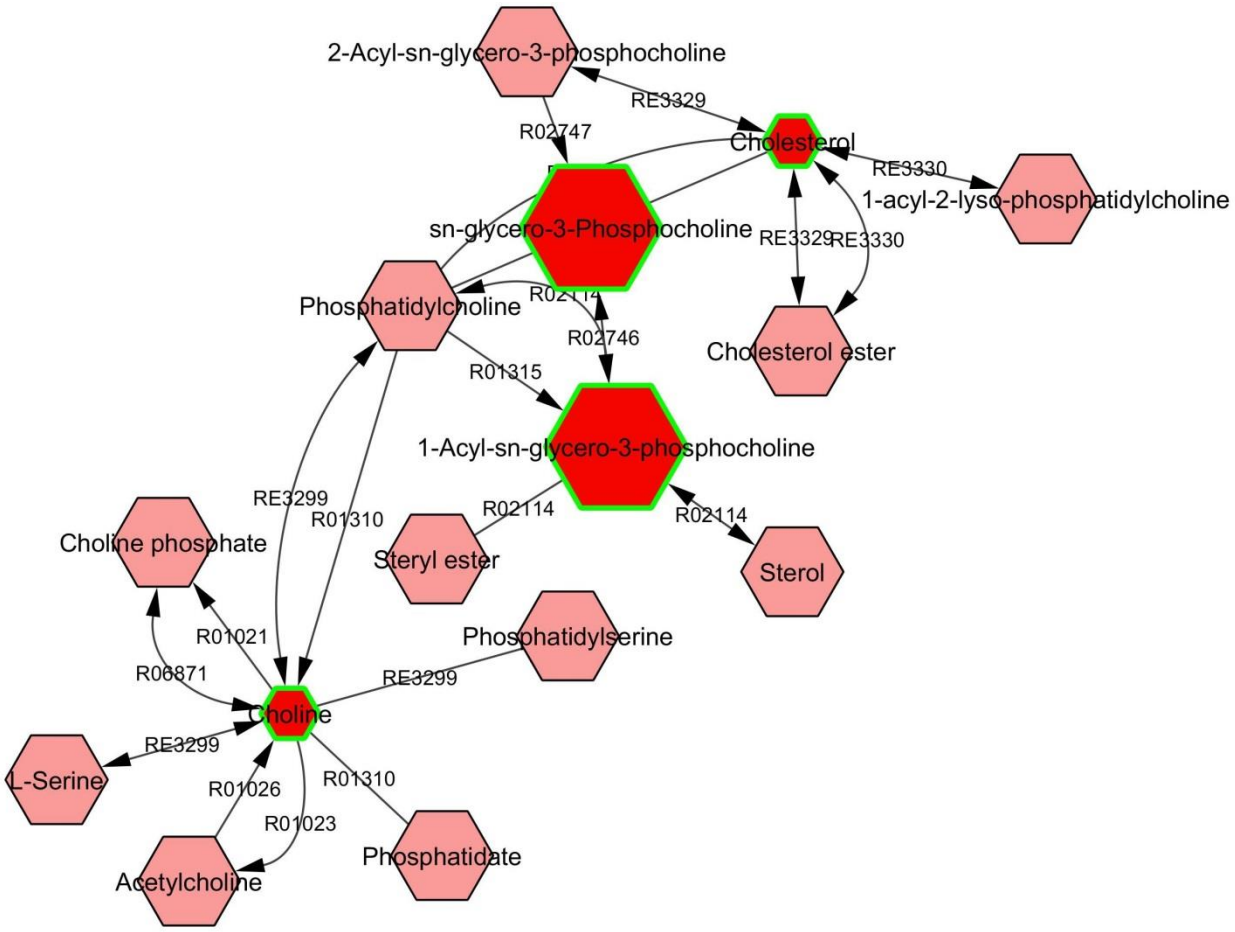


**Figure S6**. Choline metabolism of PC.

Symbols are the same as in Figure S2.

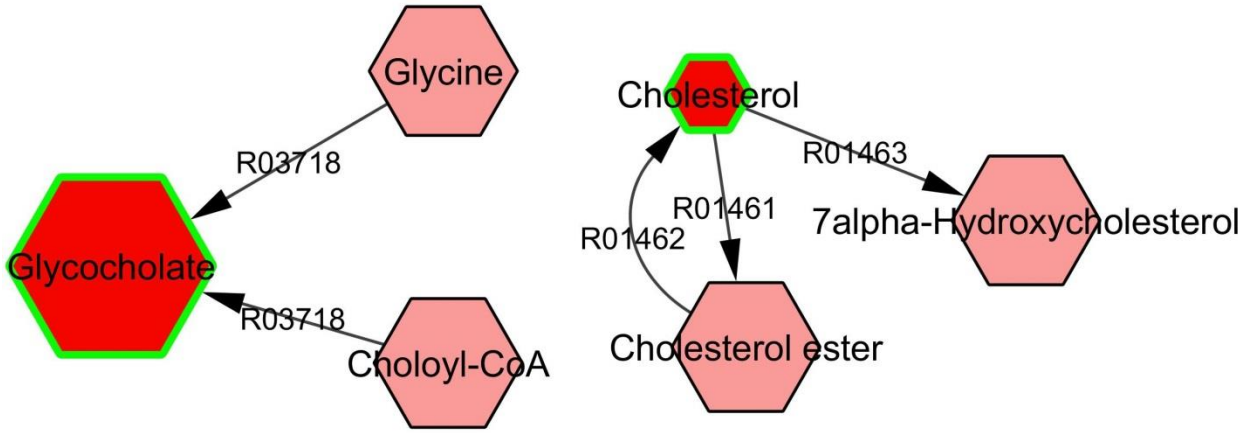


**Figure S7**. Bile acid metabolism of PC.

Symbols are the same as in Figure S2.